A STUDY ON CRITICAL FLICKER FREQUENCY IN MIGRAINEURS

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CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON CRITICAL FLICKER FREQUENCY IN MIGRAINEURS"** is the bonafide original work of **DR. K. MALCOLM JEYARAJ** in partial fulfillment of the requirements for D.M. Branch-I (NEUROLOGY) examination of THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY to be held in August 2010. The period of post-graduate study and training was from July 2007 to July 2010.

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DECLARATION

I **Dr. K. MALCOLM JEYARAJ,** solemnly declare that this dissertation entitled, **"A STUDY ON CRITICAL FLICKER FREQUENCY IN MIGRAINEURS"** is a bonafide work done by me at the Department of Neurology, Government Stanley Medical College and Hospital, Chennai during the period 2007 – 2010 under the guidance and supervision of the Professor and Head of the Department of Neurology of Government Stanley Medical College and Hospital, **Professor A. MURUGESAN**, **M.D., D.M.** This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University, towards partial fulfillment of requirement for the award of **D.M. Degree (Branch-I) in NEUROLOGY.**

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INTRODUCTION

Migraine is a condition wherein a variety of visual phenomena are frequently encountered.[6]

Migraine with and without aura involve changes in visual perceptions during an attack. [6]

Scintillations, scotomata and fortification spectra characterize the visual aura. [6] However, blurring of vision and photosensitivity are seen even among those patients who do not experience visual aura. [6]

Visual changes that occur during an attack of migraine help in clarifying the clinical picture. However, the visual response during the inter-attack period also provide valuable information. [6] Few studies that exist in this area point to differences in visual processing in migraine patient, even when they are not experiencing an attack. [6]

The human visual system processes information from the environment in three ways: spatially, temporally and chromatically. In migraine, responses to spatial stimuli have been most frequently investigated.[7,57]

Few studies have evaluated the temporal responsiveness of visual system in migraineurs. Khalil et al investigated temporal contrast sensitivity in migraineurs.[7] Coleston et al investigated temporal responsiveness of the visual system through background modulation method.[7] Critical flicker frequency is one such simple test to discern the temporal responsiveness of the visual system.

AIM OF THE STUDY

- To assess the temporal responsiveness of the visual system in migraineurs.
- To compare the critical flicker frequency in migraineurs with aura and without aura.
- To assess the temporal responsiveness of the visual system in migraineurs with visual stimuli as migraine trigger.

REVIEW OF LITERATURE

The word migraine has been derived from the ancient Greek word hemikranios which means 'half head' underscoring the unilateral distribution of head pain in many sufferers.[53]

EPIDEMIOLOGY OF MIGRAINE

THE PREVALENCE OF MIGRAINE

The estimates of migraine prevalence have varied broadly, probably because of differences in study methodology. Before puberty, migraine prevalence is higher in boys than girls. As adolescence approaches, incidence increases more rapidly in girls than boys. The prevalence increases throughout childhood and early adult life until approximately age 40, after which it declines. Overall prevalence is highest from 25 to 55, the peak years of economic productivity.[1,47,49]

In the United States, three very large studies assessed the epidemiology of migraine in adults. The American Migraine Study (AMS-1), collected information from 15,000 households representative of the US population in 1989. The American Migraine Study-II and

American Migraine Prevention & Prevalence study (AMPP) done later replicated similar methodology and found the prevalence of migraine to be around 18% in women and 6% in men. [1,36,47]

PREVALENCE BY SOCIOECONOMIC STATUS

In the United States, three very large population-based studies were conducted and they found that in the community, migraine prevalence is inversely related to household income.[31,33,34] As income or education increased, migraine prevalence declined. This inverse relationship could be explained by two alternative hypothesis. According to the social causation hypothesis, factors associated with low socioeconomic status act to increase disease prevalence. The opposing social selection hypothesis suggested that disease-related dysfunction would interfere with educational and occupational functioning, which in turn would lead to low income. The alternative hypothesis were tested in an adolescent population study.[2] In adolescents with family history of migraine, household income did not have a significant effect, probably because of the higher biological predisposition or because of a common stressor event. In those without a strong predisposition, household income was associated with prevalence. This suggested that the social causation hypothesis rather than the social

selection hypothesis was the main factor, highlighting the need for exploration of environmental risk factors related to low income and migraine and the search for specific co-morbidities and stressors in this group.[2]

THE IMPACT OF MIGRAINE ON THE INDIVIDUAL

Migraine is a public health problem of enormous scope that has an impact on both the individual and on the society.[10] The American Migraine Prevention & Prevalence study (AMPP), conducted in 2005, estimated that 35 million US residents had migraine headaches, meaning that nearly one in four US households had someone with migraine.[12] Twenty-five percent of women in the United States who had migraine experienced four or more severe attacks a month; 35% experienced one to four severe attacks a month; 38% experience one or less than one severe attack a month. Similar frequency patterns were also observed for men. Around 37% of the migraineurs had five or more headache days per month. During those attacks, most migraineurs reported severe impairment or the need for bed rest (53.7%); just 7.2% reported no attack-related impairment. Over a 3-month period, 35.1% of the migraineurs had at least one day of activity restriction related to headache.

THE IMPACT OF MIGRAINE ON THE FAMILY

Because migraine affects women more often than men and is most prevalent between the ages of 25 and 55, a substantial impact on family life might be expected. A Canadian study reported that 90% of people with migraine reported postponing their household work because of headaches, 30% had canceled family and social activities during their last migraine attack, and two-thirds feared letting others down because of their headaches. [37] Other studies[15,50] found that migraine attacks brought a significant disruption to family life, with impact on spouses, children, and friends.

In an epidemiologic study conducted in the United Kingdom and the United States, the impact of migraine on family life was assessed both from the perspective of those with migraine and from the perspective of their partners.[15] Of people with migraine living with a household partner, 85% reported substantial reductions in their ability to do household work and chores, 45% missed family, social and leisure activities, and 32% avoided making plans for fear of cancellation because of headaches. One half believed that, because of their migraine, they were more likely to argue with their partners (50%) and children (52%), whereas majorities

(52%–73%) reported other adverse consequences for their relationships with their partner and children and at work. A third (36%) believed they would be better partners but for their headaches. Participating partners partly confirmed these findings: 29% felt that arguments were more common because of headaches and 20% to 60% reported other negative effects on relationships at home. A significantly higher proportion of migraine partners were unsatisfied with work demands placed on them, with their level of responsibilities and duties and with their ability to perform. These results suggest that the impact of migraine extended to household partners and other family members.[15]

IMPACT OF MIGRAINE ON THE SOCIETY

Migraine has an enormous impact on society.[13,14, 21,41] Studies have evaluated both the indirect costs of migraine as well as the direct costs.[7,21,35] Indirect costs includes both the cost of absenteeism (missed work) and reduced productivity while at work. Hu and colleagues[21] estimated that productivity losses caused by migraine cost American employers 13 billion dollars per year.

The National Ambulatory Medical Care Survey, conducted from 1976 to 1977, found that 4% of all visits to physicians' offices (more than 10 million visits a year) were for headache.[21] Vast amounts of prescription and over-the-counter medications are taken for headache disorders. In a very recent study, Stewart and colleagues mailed a questionnaire to 193,477 participants in the American Migraine Prevalence and Prevention study. Lost productive time was the sum of missed hours plus reduced productivity hour equivalents. The mean lost productive time per week was 1.8 hours for headache and 2.8 for all health-related causes; 76.5% of the headache-related lost productive time was explained by reduced performance (ie, presenteeism). The 29% of migraine cases with 11+ headache-days per month accounted for 49% of overall lost productive time.[46]

PATHOPHYSIOLOGY OF MIGRAINE

VASCULAR HYPOTHESIS

Evidence from clinical studies and experimental evidence support the concept of abnormal intracranial and extracranial vascular reactivity in migraine and other vascular headaches. There is dilatation of scalp arteries causing increased scalp blood flow during attacks of migraine.

Similarly reduced regional flow through the cortex during the aura stage of migraine have been demonstrated through radioactive xenon cerebral blood flow studies.[53] This vascontriction – vasodilation model however has encountered a lot of difficulties. The facts against this thesis were a solid evidence from functional MRI studies that the phase of oligemia during the migraine aura is preceded by a phase of focal hyperemia.[17] The other facts against this thesis are that headache may begin while cortical blood flow is still being reduced, the oligemia that spreads across the cerebral cortex at a rate of 2 to 3mm per minute does not conform to discrete vascular territories and the headache after an aura is often on the inappropriate side. Finally migraine is also associated with premonitory phase in upto 60% of patients which would be incompatible with a vascular or ischemic hypothesis.

NEURONAL THEORIES OF MIGRAINE

The observations on spreading oligemia led to a resurgence of the central or neuronal theories of migraine. Lashley, in 1941, who studied his own scintillating scotoma, postulated on purely theoretical grounds that it must have been due to a change spreading over his occipital cortex at the rate of about 3 mm/min.[27] In 1944, Leao, during his research on

epilepsy, observed a wave of cortical electrical depression passing over the exposed brain of lower animals.[29] Activating the posterior cortex of rats started a wave of electrical depression that moved out from the point of initiation at a rate of 3 to 4 mm/min. The spreading depression noted by Leao's and Lashley's observations led to the hypothesis that the aura of migraine is primarily a neuronal event that causes the cortical circulation to close down in response to decreased metabolic requirements. There is also evidence suggesting the presence of a disturbance in energy metabolism in both the brain and extraneural tissues of patients with migraine. Based on abnormalities identified in the mitochondrial respiratory chain and matrix enzyme activities from the muscle and platelets of patients with migraine, it was proposed that the defect in brain energy metabolism is due to abnormal mitochondrial oxidative phosphorylation.[55] In addition, there is evidence to support the presence of both systemic and brain magnesium deficiency in migraineurs, particularly in the occipital lobes.[55] Magnesium normally maintains a strongly coupled state of mitochondrial oxidative phosphorylation. Magnesium also plays an important role in "gating" *N*-methyl-d-aspartate (NMDA) receptors. A magnesium deficit can therefore result in an

abnormality of mitochondrial oxidative phosphorylation and lead to a gain in NMDA receptor function, thereby causing an instability of neuronal polarization because of a loss of ionic homeostasis. This process would lead to a state of neuronal hyperexcitability and a lower threshold for spontaneous depolarization. Thus the concept of spreading depression would include a stage of spreading activation followed by spreading depression. This could explain the phenomenon of spreading oligemia being preceded by focal hyperemia. These findings taken together suggest that the changes in blood vessel caliber and blood flow may be due to a primary neuronal event, triggered by enhanced neuronal excitability and susceptibility to spontaneous depolarization, resulting in prolonged hypometabolism because of an impairment in energy metabolism caused by mitochondrial dysfunction. This hypothesis has also been supported by the finding of increased interictal lactate levels in the occipital cortex of migraineurs using proton MRS.[54] The theory that the migraine aura is a primary neuronal event was further strengthened by another study, which demonstrated no change in the apparent diffusion coefficient on diffusion-weighted MRI despite a reduction of regional cerebral blood flow during spontaneous migraine aura. Because diffusion-weighted MRI

is very sensitive to tissue ischemia, the researchers concluded that the reduction in cerebral blood flow was not of sufficient magnitude to cause tissue ischemia.[9]

VISUAL SYSTEM DYSFUNCTION AND CRITICAL FLICKER FREQUENCY IN MIGRAINEURS

There are few studies which have used psychophysical methods to examine the functional status of the visual pathways. Coleston and co-workers have utilized tests to assess the magnocellular and parvocellular pathways.[7] In their experiment the ST-1 spatial response was obtained by measuring the threshold target illumination at which the subject could just detect a target moving back and forth across a square-wave background grating. In this experiment they used a range of background frequencies and obtained a characteristic curve which reflected the functioning of X-type (ie. parvocellular) neurons. The ST-2 temporal response curve was obtained in a similar manner but the background was modulated in the temporal rather than in the spatial domain. The ST-2 responses reflected the Y-type (i.e., magnocellular) function. They evaluated ST-1 & ST-2 responses in migraine with aura, migraine without aura and matched controls.[7] In the ST-1 experiment, the background spatial frequency at

which the threshold target illumination peaked was lower for both groups of migraineurs than for controls. In the ST-2 data, the background temporal frequency at which the threshold target illumination peaked was also slightly lower for migraineurs than for controls. Through this study, Coleston and co-workers provided some evidence to suggest that the functioning of the visual pathways is impaired in migraineurs during inter-attack period. Coleston et al suggested three pathophysiological possibilities for the same. First being, some intrinsic abnormality of the magnocellular and parvocellular pathways in migraine. Secondly, the functional integrity of the pathways would in some ways be directly compromised by repeated migraine attacks. Thirdly, they postulated that given the existence of rich back projections from the striate cortex to the lateral geniculate nuclei, the cortical disruptions of the migraine attack could cause retrograde geniculate disturbances.

Critical flicker frequency is one such quick simple test to assess the temporal responsiveness of the visual system. The sensitivity threshold is measured. Coleston and Kennard have examined the critical flicker frequencies of migraineurs with and without aura and controls.[6] Kowacs et al have also examined the critical flicker frequencies as a

function of the temporal responsiveness of the visual system in migraineurs.[23] Kowacs et al have concluded in their experiment that critical flicker frequency was the lowest in migraineurs with aura.[23]

THE PRIMARY VISUAL CORTEX

The primary visual cortex in migraine patients has recently been focus of a number of psychophysical investigations. A number of studies have involved the use of high contrast square-wave grating stimuli of intermediate fundamental spatial frequency. Wilkins et al have reported that patients with unilateral headache were more likely to report asymmetric illusions in a 4 cycles/ degree grating pattern.[56,57] Marcus and Soso in their experiment also found that migraineurs were significantly more averse to gratings than were the control subjects.[38]

Khalil used patients with diagnosed migraine and reported that (i) overall, migraineurs saw more illusions than control subjects, regardless of the size of the stimulus. (ii) migraineurs experienced more discomfort on viewing the patterns than did controls. (iii) illusions and discomfort were more frequent in those suffering migraine with aura than those without aura. (iv) patients with unilateral aura saw more illusions on the aura side than on the contralateral side, and those with frequent (1

per week) migraine attacks tended to see more illusions than those with infrequent attack (5-10 per year).[30] Coleston and Kennard used a slightly different approach in that they asked the patients to rate the intensity of the illusions they saw, rather than simply listing them. Patients with aura reported significantly more intense illusions over a range of spatial frequencies than did patients without aura.[8]

Other psychophysical methods employed to assess spatial and temporal contrast sensitivity were determined by Khalil. Both were significantly reduced in migraine with aura, but not migraine without aura, as compared to the control group. In addition, in the migraine with aura group only, Khalil reported a significant relationship between migraine chronicity and spatial contrast sensitivity.[8]

In general, psychophysical research examining visual cortical functioning in migraine has consistently suggested a hypersensitivity in migraine with aura patients but not in those without aura.[5]

MIGRAINE TRIGGERS

Though clinical evidence suggests that migraine may be triggered by visual stimuli, scientific evidence regarding visually triggered attacks is minimal.[11]

Estimates regarding visual triggers of migraine vary widely. Van den bergh et al implicated visual triggers in only 2.7% of study population.[51] However Robbins et al discovered that bright light or sunlight was a leading trigger factor (38% of all patients).[44]

The mechanism of a visually triggered migraine is not very well known. The possible mechanisms could be whether visual stimuli in isolation are sufficient (as in photosensitive epilepsy) or whether an interaction between visual stimuli and other situational factors is required or whether there is any visual system dysfunction in these patients.[5]

Hay et al have examined the types of visual stimuli to which migraine patients are subjectively sensitive : the three most common are glare, flicker and alternate light and shade.[18] Despite the above observations there are certain clear links between visual stimuli and the aura and they are (1) aura symptoms are most commonly visual. (2) neuronal spreading depression has been strongly implicated in the pathophysiology of aura phase[27] and (3) animal models have shown appropriate visual stimulation (flickering light) can elicit cortical depression.[52] In human migraine, flickering light is often cited by patients as an effective trigger.[11,18]

PHOTOPHOBIA

Photophobia accompanies migraine frequently. Photophobia may occur in two forms. The first a true photophobia i.e., pain induced (or) exacerbated by exposure to bright light and the other being a sense of glare (or) dazzle.[5]

Painful photophobia depends on the functional integrity of both the optic and trigeminal nerve and may result from the interaction of an appropriate light stimulus and ophthalmic nerve irritation. Apart from this pain, blepharospasm and lacrimation may be recorded. The postulated mechanism behind the photophobia is postulated to be trigeminal / trigeminovascular activation.[5]

Dazzle as distinct from true photophobia is thought to be based either on diffusion of light in the ocular media or on a lack of adaptation.[5]

MIGRAINE AURA

The migraine aura has been defined as a focal neurological disturbance manifested as visual, sensory (or) motor symptoms.[19] It is seen in around 30% of patients.[42] The case for the aura being the human equivalent of the cortical spreading depression of Leao has been suggested.[29,39] The visual aura has been described to affect the visual

field, suggesting the visual cortex and this starts at the centre of the visual field propagating to the periphery at the rate of 3 mm / min.[27] This is very similar to the spreading depression observed in rabbits.[29] Blood flow studies in patients as described earlier shows a focal hyperemia tending to precede the spreading oligemia.[40] This is a phenomenon expected to occur in spreading depression. Thus human observations suggest that human aura has its equivalent in animals cortical spreading depression.[3]

Recent evidence has also suggested that Tonaberasat a cortical spreading depression inhibitor has entered clinical trials in migraine. The postulated mechanism of action of Tonaberasat is that it inhibits cortical spreading depression and cortical spreading depression induced nitric oxide release and cerebral vasodilation.[16,43,48]

MECHANISM OF HEADACHE

The limitation of the migraine attack though it arises in the nervous system, is that it does not adequately explain the mechanism of headache. The pain sensitive intracranial structures include large blood vessels, duramater and large venous sinuses which are innervated by a plexus of largely unmyelinated fibres that arise from the ophthalmic branch of the trigeminal nerve. Once the trigeminovascular system is activated,

impulses are transmitted centrally toward the first synapse within lamina I and II_0 of the trigeminal nucleus caudalis which extends to the dorsal horn of C2-3. From this point, nerve impulses travel rostrally to the cortex via thalamic relay centers. Once activated trigeminal nociceptive afferents can generate neurogenic inflammation via antidromic release of neuropeptides from the axonal terminal of nociceptive trigeminal fibres that innervate meningeal blood vessels. The Trigeminal nuclear complex also receives impulses from trigeminal vascular afferents which are activated by sterile perivascular neurogenic inflammation.[53]

CLINICAL FEATURES OF MIGRAINE

Migraine attacks as discussed earlier have been separated into those that are and those that are not accompanied by transient focal neurological symptoms known as the aura. The two types are not mutually exclusive, and many patients have attacks of each type. The headache phase of migraine with and without aura is similar and typically consists of episodes of unilateral throbbing head pain of moderate to severe intensity that, if untreated, persists from 4 hours up to 3 days and tends to worsen with routine levels of physical exertion. Migraine attacks tend to be accompanied by nausea, vomiting, and light or sound

sensitivity, although not every patient experiences all of these symptoms.[19]

MIGRAINE WITHOUT AURA

Migraine without aura occurs episodically and is not preceded or accompanied by any identifiable neurological symptoms due to focal cerebral or brainstem disturbances. Many patients with migraine report that their headaches are preceded by a prodromal phase that would consist of alterations in mood or energy level, excessive yawning, thirst, or food cravings. After these premonitory warnings, the headache would occur within hours or during the next day. The attack may awaken the subject during the night, but more commonly the patient awakens near to the normal time to find that the attack has already started. At this stage, the pain may be unilateral and is usually supraorbital, but it may be holocephalic. An initially unilateral headache may progress to generalized head pain, or it may switch to the contralateral side during the course of the attack. Headache arising frontally can radiate or migrate posteriorly or vice versa. Patients with migraine may have attacks that primarily affect the cheek, ear, nose, or neck. These attacks, sometimes called lower-half headaches, would generally be considered in patients

with facial pain accompanied by nausea, vomiting, and photophobia. Pain in the lateral portion of the neck with tenderness over the carotid artery may be found in lower-half headaches.[53]

The quality of the pain of migraine is often described as throbbing (pulsatile), although in some patients the throbbing nature of pain would occur only with more severe attacks. Many patients, would however, describe the pain as steady while they remain still. It tends to pulsate or throb at the heart rate with exertion, after a Valsalva maneuver, or during the head-low position; however, a description of throbbing pain during migraine attacks is not mandatory for a diagnosis. In general, during acute attacks migraineurs would wish to remain as still as possible and prefer a dark quiet room.[53]

Other symptoms are often associated with the pain of migraine. Photophobia and phonophobia are common and osmophobia (sensitivity to smells) may also occur. The onset of nausea and vomiting in migraine can occur almost as soon as the pain develops, but it is more commonly delayed until the attack has been in progress for 1 hour or longer. The gastrointestinal symptoms can include diarrhea. Blurred vision is a common complaint during all types of migraine. Lightheadedness is also

common and may progress to syncope in a small percentage of patients. Subconjunctival hemorrhages, orbital ecchymoses, and epistaxis have all been uncommonly reported to accompany migraine. Although fever, tachycardia and paroxysmal atrial tachycardia are rare migraine-related symptoms, possibly due to associated disturbances of the autonomic nervous system, their presence requires investigation of other possible causes for headache, such as infection or intracranial hemorrhage.[53] The pain of a migraine attack tends to build up to a peak over 30 minutes to several hours. Rarely the onset is described as being more explosive. The attack generally lasts several hours to a full day. Severe episodes can continue for days and, if associated with vomiting, can lead to prostration and dehydration. Very prolonged, severe attacks lasting longer than 72 hours are called *status migrainosus* and may warrant admission to the hospital for pain relief and correction of fluid and electrolyte imbalance. More commonly, the attack subsides within a day or after a night's sleep. The day after the intense pain, the patient feels tired and listless. The frequency and severity of episodes of migraine without aura are extremely variable both from patient to patient and over time within an individual patient. Recurrence of attacks one to four times per month is

not uncommon, and attacks in relation to the menstrual cycle are a common pattern in women during the reproductive years. Attacks at less than weekly intervals are common in patients who attend neurology clinics and may indicate that a chronic daily headache pattern is evolving.

MIGRAINE WITH AURA

In migraine with aura, periodic headaches are preceded or accompanied by an aura which would consist of transient visual, sensory, or language disturbance or other focal cerebral or brainstem symptoms. Aura occurs in about 15% to 20% of migraineurs and generally does not occur in every attack. Although each of the aura types may occur alone in a given attack, in some individuals they can occur sequentially. Usually, the visual disturbance is followed by sensory symptoms and then in turn by language symptoms. When this occurs, the headache may overlap one or more of the later-appearing aura symptoms. The pain is identical to that of migraine without aura but is unilateral in a higher percentage of patients.

The most common aura is the disturbance of vision known as a scintillating scotoma (teichopsia). This generally begins as a shimmering arc of white or colored lights in the left or right visual field

homonymously. The arc of light gradually enlarges and it may have a definite zigzag pattern. It may be a single band of light or may have a much more complex pattern. It has a shimmering or flickering quality. Gradually, over the course of a few minutes, the scintillating pattern expands from the point just lateral to fixation to involve a quadrant or hemifield of vision in both eyes. Commonly, the positive scotoma is followed by a spreading zone of vision loss (negative scotoma). [53]

The scotoma usually originates in the calcarine cortex of one cerebral hemisphere and should therefore be an essentially congruent homonymous field defect; however, it is sometimes described as being seen in one eye only or as being worse on one side than the other. Patients often describe the visual disturbance in vague terms, such as “blurry vision,” “double vision,” or “jumpy vision. There are many variations of migrainous teichopsia (subjective visual images). The zigzag appearance may be so pronounced to justify the term fortification spectrum because of its fanciful resemblance to the ground plan of a fort. Occasionally, the scotoma is less complex and is simply described as a ball of light in the center of the visual fields. It may obscure vision to a significant degree. This type of teichopsia may represent a bilateral calcarine disturbance. [53]

The teichopsia of migraine may be more complex and formed than the usual lines and geometric patterns. Disturbances of this complex type may be due to dysfunction in the posterior temporal lobe. Changes in the perception of the shape or form of viewed objects (metamorphopsia) can lead to frightening and bizarre visual hallucinations.

Visual disturbances due to retinal dysfunction are relatively uncommon in migraine and may take the form of unilateral flashes of light (photopsia), scattered areas of vision loss, altitudinal defects, or even transient unilateral vision loss. When such monocular visual disturbances are followed by a headache, the term retinal migraine would appropriate.

When the photopsia, teichopsia, and other disturbances are seen in both visual fields simultaneously, they probably originate from the calcarine cortex. A homonymous visual aura is generally followed by a headache on the contralateral side of the head.

Sensory aura, the second most common aura type, is, like the visual aura, characterized by positive symptoms (paresthesias) followed by negative symptoms (numbness), which slowly spread or migrate.

Paresthesias can occur, alone or in conjunction with one of the previously described visual symptoms. The numbness or tingling may be felt in almost any distribution, from a hemisensory disturbance to one that involves all four limbs or a much more restricted area, such as the lips, face, and tongue. The paresthesias usually last from 5 minutes to 20 to 30 minutes. The paresthesias of migraine aura seem to have a predilection for the face and hands. The rate of spread of a sensory aura is important to help distinguish it from a sensory seizure and the sensory disturbance of a transient ischemic attack. A migrainous sensory aura generally resolves over the course of 20 to 60 minutes. After the aura there is usually a latent period of a few minutes before the onset of the headache. In some subjects, the aura and the headache merge. [53]

After sensory aura, the next most common type is the language aura. Aphasia can occur as the aura of migraine. The aphasia, which is usually mild and transient, can be either an expressive or a receptive type. The ensuing headache generally resembles headaches the patient has had in the past and that followed the more typical visual aura.

Weakness of the limbs or facial muscles on one side of the body occurs only rarely as a motor aura in migraine. Although traditionally considered a form of aura, the most recent edition of the International Headache Society diagnostic criteria now classifies motor aura separately as hemiplegic migraine based on the increasing information relating to the genetic involvement of migraine with motor symptoms.[19] The weakness generally lasts 20 to 30 minutes.

MIGRAINE AURA WITHOUT HEADACHE

When a visual, sensory, motor, or psychic disturbance characteristic of migraine aura is not followed by headache, the episode is termed migraine aura without headache. Most commonly encountered in patients who have a past history of migraine with aura, the episodes can also begin de novo. Migraine equivalents are easily recognized when the attacks occur on a background of migraine with aura. In the absence of such a history, the transient disturbance may be difficult to distinguish from an episode of transient cerebral or brainstem ischemia.[19,53]

CLASSIFICATION OF MIGRAINE

Migraine is now classified according to the scheme devised by Second Headache Classification Committee of the International Headache Society (Headache Classification Committee, 2004).[19] The classification is as follows :

1.1. Migraine without aura

1.2. Migraine with aura

1.2.1. Typical aura with migraine headache

1.2.2. Typical aura with nonmigraine headache

1.2.3. Typical aura without headache

1.2.4. Familial hemiplegic migraine

1.2.5. Sporadic hemiplegic migraine

1.2.6. Basilar-type migraine

1.3 Childhood periodic syndromes that are commonly precursors of migraine

1.3.1. Cyclical vomiting

1.3.2. Abdominal migraine

1.3.3. Benign paroxysmal vertigo of childhood

1.4 Retinal migraine

1.5 Complications of migraine

1.5.1. Chronic migraine

1.5.2. Status migrainosus

1.5.3. Persistent aura without infarction

1.5.4. Migrainous infarction

1.5.5. Migraine-triggered seizures

1.6 Probable migraine

1.6.1 Probable migraine without aura

1.6.2 Probable migraine with aura

1.6.3 Probable chronic migraine

DIAGNOSTIC CRITERIA FOR MIGRAINE[19]

The diagnostic criteria for migraine with and without aura as per the Second Headache Classification Committee of the International Headache Society[19] is as follows :

1.1 Migraine without aura

Previously used terms are common migraine and hemicrania simplex.

Description

Recurrent headache disorder manifesting in attacks lasting 4-72 hours. Typical characteristics of the headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity and association with nausea and/or photophobia and phonophobia.

Diagnostic criteria

A. At least 5 attacks fulfilling criteria B-D
B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
C. Headache has at least two of the following characteristics:
    1. unilateral location
    2. pulsating quality
    3. moderate or severe pain intensity
    4. aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
D. During headache at least one of the following:
    1. nausea and/or vomiting

2. photophobia and phonophobia

E. Not attributed to another disorder

1.2.1 Typical aura with migraine headache

Description

Typical aura consisting of visual and/or sensory and/or speech symptoms. Gradual development, duration no longer than one hour, a mix of positive and negative features and complete reversibility characterise the aura which is associated with a headache fulfilling criteria for 1.1 Migraine without aura**.**

Diagnostic criteria

A. At least 2 attacks fulfilling criteria B-D

B. Aura consisting of at least one of the following, but no motor weakness:

    1. fully reversible visual symptoms including positive features (eg, flickering lights, spots or lines) and/or negative features (ie, loss of vision)

2. fully reversible sensory symptoms including positive features (ie, pins and needles) and/or negative features (ie, numbness)
3. fully reversible dysphasic speech disturbance

C. At least two of the following:
1. homonymous visual symptoms and/or unilateral sensory symptoms
2. at least one aura symptom develops gradually over ≥ 5 minutes and/or different aura symptoms occur in succession over ≥ 5 minutes
3. each symptom lasts ≥ 5 and ≤ 60 minutes

D. Headache fulfilling criteria B-D for 1.1 Migraine without aura begins during the aura or follows aura within 60 minutes

E. Not attributed to another disorder

DISABILITY IN MIGRAINE

World Health Organisation defines the functional consequences of illness in terms of impairment, functional limitations and disability. Disability refers to the consequences of illness on ability to work and function in other roles. To help improve the assessment of headache

related disability Migraine Disability Assessment Questionnaire (MIDAS) was developed. MIDAS (see Annexure II) is a simple 5 item questionnaire to assess the lost time from work for pay, housework or chores and leisure activities. MIDAS is a sum of the number of lost days in these three domains.

MATERIALS & METHODS

The study was conducted on migraine patients attending neurology out-patient department at Government Stanley Medical College. This is an observational study done prospectively. It was a one point in time study. The study was approved by the Ethics Committee, Government Stanley Medical College, Chennai. The study population consisted of three groups. The first group was thirty individuals who satisfied the Second Headache Classification Committee of the International Headache Society (Headache Classification Committee, 2004)[19] criteria for diagnosis of migraine with aura. The second group was thirty individuals who satisfied the Second Headache Classification Committee of the International Headache Society (Headache Classification Committee, 2004) criteria for migraine without aura. The third group was thirty individuals without a history of migraine – control group. Informed consent was obtained from each individual.

Exclusion criteria consisted of patients who have underlying ocular disorder other than refractory errors, presence of other neurological

diseases, lack of capacity to understand or to co-operate with the study, abnormalities in neuroimaging and history of chronic hypertension.

A detailed proforma (See Annexure I) was prepared which included details regarding headache history, height, weight, occupation of the subject, hours of computer usage, family history of migraine, past medical and surgical history and chronic medication usage. Two blood pressure recordings were obtained from the right arm of the patient in supine posture and the mean was calculated.

The subjects were then subjected to critical flicker frequency measurement. Patients were first instructed and trained about the procedure. Flicker frequencies were measured eight times and the mean value was calculated. The critical flicker frequency measurement was carried out under dim light. The whole procedure took about fifteen minutes. A portable hand held flicker box was used to produce the temporal stimulus. Critical flicker frequency threshold was measured by intrafoveal stimulation with a luminous diode. Decreasing the frequency of the light pulses from 60 Hz downward, the critical flicker frequency threshold was determined as the frequency when the impression of fused light turned to a flickering one. Both the study groups and the controls

were tested for the critical flicker frequency during the headache free period. Differences in the critical flicker frequency between the study groups and controls were measured.

Statistical Analysis

The demographic variables are given frequencies with their percentages. The critical flicker frequency values are given in mean and standard deviation. The qualitative data were analysed using Pearson chi square test. The quantitative data were analysed using student independent t-test. The one way ANOVA test was also used. The migraineurs with aura, without aura and control, mean critical flicker frequency differences were analysed using student independent t-test. P value less than 0.05 was taken as significant.

OBSERVATION AND RESULTS

The study was done on patients attending the neurology out patient department at Government Stanley Medical College, Chennai. The total number of subjects chosen for the study were 30 patients of migraine with aura, 30 patients of migraine without aura and 30 controls.

Table 1 : Comparison of mean age of migraineurs with aura, without aura and controls

Group		N	Mean	Standard Deviation	Oneway ANOVA F-test
Visual Aura	Present	30	28.60	9.175	F=0.15 p=0.86
	Absent	30	27.30	9.883	
Control		30	28.10	8.430	
Total		90	28.00	9.094	

Comparison of mean age of migraineurs with aura, without aura and controls is shown in Table 1.

The mean age of migraineurs with aura is 28.60+/-9.175. The mean age of migraineurs without aura is 27.30+/-9.883. The mean age of control population is 28.10+/-8.430. The difference in the age groups is not statistically significant($p>0.05$). Hence it can be inferred that age is not a confounding factor in the analysis of critical flicker frequency among the three subgroups.

Table 2 : Age of onset of migraine in study subjects

Group		N	Mean	Standard Deviation	Student independent t-test
Visual aura	Present	30	26.30	9.018	t=0.99 p=0.32
	Absent	30	24.00	8.871	
	Total	60	25.15	8.944	

Table 2 illustrates the age of onset (years) of migraine in subjects with and without aura.

The mean age of onset of migraine in subjects with aura is 26.30+/- 9.018 and the mean age of onset of migraine in subjects without aura is 24+/-8.871. The difference in the age of onset of migraine in subjects with and without aura was not statistically significant ($p > 0.05$).

Table 3 : Duration of migraine in study subjects

Group		N	Mean (years)	Standard Deviation	Student independent t-test
Visual Aura	Present	30	2.41	1.211	t=2.71 p=0.009
	Absent	30	3.50	1.796	

The duration of migraine (years) in migraineurs with and without aura is shown in Table 3.

The mean duration of migraine in subjects with aura is 2.41+/- 1.211 and the mean duration of migraine in subjects without aura is 3.50+/- 1.796. The mean duration of migraine in subjects with and without aura were compared and the difference is statistically significant ($p<0.05$). The mean duration of migraine was more in the migraineurs without aura study group.

Table 4 : Average number of migraine episodes per month

Group		N	Mean	Standard Deviation	Student independent t-test
Visual aura	Present	30	4.07	1.760	t=2.71 p=0.009
	Absent	30	3.37	1.426	

Table 4 shows the average number of days of migraine episodes per month in migraineurs with and without aura.

The mean number of migraine episodes per month in migraine subjects with aura is 4.07+/-1.760. The mean number of migraine episodes per month in migraine subjects without aura is 3.37+/-1.426. The difference in the mean number of episodes per month in migraineurs with aura versus migraineurs without aura is statistically significant ($p<0.05$).

Table 5 : Migraineurs with family history of migraine

Family History	Group				Chi-square test
	With Aura		Without Aura		
	n	%	n	%	
Absent	26	86.7%	27	90.0%	$\chi 2$=0.16 p=0.68
Present	4	13.3%	3	10.0%	

Study subjects with family history of migraine is shown in Table 5.

The presence of family history of migraine in subjects with aura subgroup is 13.3%. The presence of family history in those without aura is 10%. The difference is not statistically significant ($p>0.05$).

Table 6 : Duration of headache in migraineurs

Group		N	Mean (hours)	Standard Deviation	Student independent t-test
Duration of migraine	With aura	30	8.37	4.491	t=1.16 p=0.24
	Without aura	30	7.20	2.976	

Table 6 illustrates the average duration of headache in hours, in migraineurs with and without aura.

The mean duration of headache in migraineurs with aura is 8.37+/-4.491. The mean duration of headache in migraineurs without aura is 7.20+/-2.976. Even though there is an observed difference of 1.27 hours, it is not statistically significant($p>0.05$).

Table 7 : Mean critical flicker frequency in migraineurs and controls

Group		N	Mean	Standard Deviation	One way ANOVA F-test
Visual Aura	Present	30	40.363	0.8838	F=265.9 p= 0.001
	Absent	30	42.227	0.5017	
Control		30	45.663	1.1898	

Table 7 explains the mean critical flicker frequency (Hertz) in migraineurs with aura, without aura and controls.

The mean critical flicker frequency in migraineurs with aura is 40.363+/- 0.8838. The mean critical flicker frequency in migraineurs without aura is 42.227+/-0.5017. The mean critical flicker frequency in controls is 45.663+/-1.1898.

Table 8 : Mean critical flicker frequency in migraineurs with aura and controls

Group	N	Mean	Standard Deviation	Student independent t-test
With Aura	30	40.363	0.88	t=19.58 p=0.001
Control	30	45.663	1.18	

Table 8 compares the critical flicker frequency (Hertz) in migraineurs with aura and controls.

The mean critical flicker frequency in migraineurs with aura is 40.363+/-0.88. The mean critical flicker frequency in controls is 45.663+/- 1.18. The difference in mean critical flicker frequency in migraineurs with aura versus controls is statistically significant ($p<0.05$). Hence, it can be inferred that the temporal responsiveness of the visual system is lowered in migraineurs with aura.

Table 9 : Mean critical flicker frequency in migraineurs without aura and controls

Group	N	Mean	Standard Deviation	Student independent t-test
Without Aura	30	42.227	0.50	t=14.57 p=0.001
Control	30	45.663	1.18	

Table 9 illustrates the critical flicker frequency (Hertz) in migraineurs without aura and controls.

The mean critical flicker frequency in migraineurs without aura is 42.227+/-0.50. The mean critical flicker frequency in controls is 45.663+/- 1.18. The difference in mean critical flicker frequency in migraineurs without aura versus controls is statistically significant ($p<0.05$). Thus the critical flicker frequency is lower in migraineurs without aura.

Table 10 : Mean critical flicker frequency in migraineurs with and without aura

Group		N	Mean	Standard Deviation	Student independent t-test
Visual Aura	Present	30	40.363	0.88	t=10.04
	Absent	30	42.227	0.50	p=0.001

The mean critical flicker frequency(Hertz) in migraineurs with and without aura is shown in Table 10.

The mean critical flicker frequency in migraineurs with aura is 40.363+/-0.88. The mean critical flicker frequency in migraineurs without aura is 42.227+/-0.50. The observed difference in mean critical flicker frequency in migraineurs with and without aura is statistically significant ($p<0.05$). Hence it can be inferred that the temporal responsiveness of the visual system is lower in migraineurs with aura compared to migraineurs without aura.

Table 11 : Comparison of critical flicker frequency in migraineurs with aura subgroup among those with MIDAS score 1,2 versus 3,4

Group	N	Mean	Standard Deviation	Student independent t-test
Midas 1,2	22	40.764	0.6536	t=9.03 p=0.001
Midas 3,4	8	39.263	0.2560	

Table 11 explains the mean critical flicker frequency (Hertz) of migraineurs with aura among patients who have a MIDAS score of 1 and 2 versus 3 and 4.

The mean critical flicker frequency of migraineurs with aura with a MIDAS score of 1 and 2 is 40.764+/-0.6536. The mean critical flicker frequency of migraineurs with aura with a MIDAS score of 3 and 4 is 39.263+/-0.2560. The observed difference is statistically significant ($p<0.05$). Hence it can be inferred that among migraineurs with aura, those who had moderate to severe disability also had impaired temporal responsiveness of the visual system.

Table 12 : Comparison of critical flicker frequency in those with MIDAS score 1,2 versus 3,4 in migraineurs without aura

Group	N	Mean	Standard Deviation	Student independent t-test
Midas 1,2	26	42.365	0.3498	t=5.44
Midas 3,4	4	41.325	0.4031	p=0.001

The mean critical flicker frequency(Hertz) of migraineurs without aura among patients who have a MIDAS score of 1 and 2 versus 3 and 4 is shown in Table 11.

The mean critical flicker frequency of migraineurs without aura with a MIDAS score of 1 and 2 is 42.365+/-0.3498. The mean critical flicker frequency of migraineurs without aura with a MIDAS score of 3 and 4 is 41.325+/-0.4031. The difference is statistically significant ($p<0.05$). Thus, among migraineurs without aura, those who had MIDAS score of 3 and 4 had a lower critical flicker frequency.

Table 13 : Comparison of critical flicker frequency in migraineurs with and without aura among patients with MIDAS score 1 and 2

Group		N	Mean	Standard Deviation	Student independent t-test
Visual Aura	Present	22	40.764	0.6536	t=10.31 p=0.001
	Absent	26	42.365	0.3498	

Table 13 illustrates the mean critical flicker frequency (Hertz) in migraineurs with and without aura among patients who had MIDAS score of 1 and 2.

The mean critical flicker frequency of migraineurs with aura with a MIDAS score of 1 and 2 is 40.764+/-0.6536. The mean critical flicker frequency of migraineurs without aura with a MIDAS score of 1 and 2 is 42.365+/-0.3498. The difference is statistically significant ($p<0.05$). Hence it can be inferred that even among migraineurs with a MIDAS score of 1 and 2, those in the aura subgroup had a lower critical flicker frequency.

Table 14 : Migraineurs with MIDAS score 3 and 4 : comparison of critical flicker frequency in those with and without aura

Group		N	Mean	Standard Deviation	Student independent t-test
Visual Aura	Present	8	39.263	0.2560	t=10.94
	Absent	4	41.325	0.4031	p=0.001

The mean critical flicker frequency(Hertz) in migraineurs with and without aura among patients who had MIDAS score of 3 and 4 is explained in Table 14.

The mean critical flicker frequency of migraineurs with aura with a MIDAS score of 3 and 4 is 39.263+/- 0.2560. The mean critical flicker frequency of migraineurs without aura with a MIDAS score of 3 and 4 is 41.325+/-0.4031. The observed difference is statistically significant ($p<0.05$). Thus among Migraineurs with a MIDAS score of 3 and 4, those in the aura subgroup had a lower critical flicker frequency.

Table 15 : Critical flicker frequency in migraineurs with and without visual trigger among the aura subgroup

Group		N	Mean	Standard Deviation	Student independent t-test
Visual trigger	Present	10	39.520	0.4733	t=4.99 p=0.001
	Absent	20	40.785	0.7242	

Critical flicker frequency(Hertz) in migraineurs with and without a visual trigger among the aura subgroup is explained in Table 15.

The mean critical flicker frequency among patients who had a visual trigger at the onset of migraine is 39.520+/-0.4733. The mean critical flicker frequency among patients who did not have a visual trigger at the onset of migraine is 40.785+/-0.7242. The observed difference is statistically significant($p<0.05$). Hence it can be inferred that among migraineurs with aura those who had a visual trigger at the onset of migraine had a lower mean critical flicker frequency.

Table 16 : Comparison of critical flicker frequency in those with and without visual trigger among migraineurs without aura

Group		N	Mean	Standard Deviation	Student independent t-test
Visual trigger	Present	7	41.686	0.5757	t=4.02
	Absent	23	42.391	0.3463	p=0.001

Table 16 compares the critical flicker frequency(Hertz) in those patients with and without a visual trigger among migraineurs without aura subgroup.

The mean critical flicker frequency among subjects who had a visual trigger at the onset of migraine is 41.686+/-0.5757. The mean critical flicker frequency among subjects who did not have a visual trigger at the onset of migraine is 42.391+/-0.3463. The observed difference is statistically significant($p<0.05$). Thus among migraineurs without aura the critical flicker frequency was lower in subjects who had a visual trigger at the onset of migraine.

Table 17 : Comparison of critical flicker frequency in migraineurs with and without aura among subjects with visual trigger at the onset of migraine

Group		N	Mean	Standard Deviation	Student independent t-test
Visual aura	Present	10	39.520	0.4733	t=8.51 p=0.001
	Absent	7	41.686	0.5757	

Table 17 compares the critical flicker frequency (Hertz) of migraineurs with and without aura among subjects with visual trigger at the onset of migraine.

The mean critical flicker frequency among migraineurs with aura is 39.520+/-0.4733. The mean critical flicker frequency among migraineurs with aura is 41.686+/-0.5757. The difference is statistically significant($p<0.05$). Thus among subjects who had a visual trigger at the onset of migraine, those with aura had a lower critical flicker frequency.

Table 18 : Comparison of critical flicker frequency in those with and without computer usage among migraineurs with aura

Group	N	Mean	Standard Deviation	Student independent t-test
Computer Users	6	40.233	0.8710	t=0.39
Computer Non Users	24	40.396	0.9024	p=0.69

Table 18 compares the critical flicker frequency (Hertz) in those with and without computer usage among migraineurs with aura.

The mean critical flicker frequency among those with computer usage were 40.233+/-0.871. The mean critical flicker frequency among those without computer usage were 40.396+/-0.9024. The observed difference was not statistically significant ($p>0.05$). Thus computer usage did not significantly alter the temporal responsiveness of the visual system.

Table 19 : Critical flicker frequency in computer users versus computer non users among migraineurs without aura

Group	N	Mean	Standard Deviation	Student independent t-test
Computer Users	6	42.450	0.7944	t=1.23
Computer Non Users	24	42.171	0.4048	p=0.22

Table 19 explains the critical flicker frequency (Hertz) in those with and without computer usage among migraineurs without aura.

The mean critical flicker frequency among those with computer usage were 42.45+/-0.7944. The mean critical flicker frequency among those without computer usage were 42.171+/-0.4048. The observed difference was not statistically significant($p>0.05$). Thus computer usage did not significantly alter the temporal responsiveness of the visual system in migraineurs without aura.

Table 20 : Comparison of critical flicker frequency among computer users in migraineurs with and without aura

Group		N	Mean	Standard Deviation	Student independent t-test
Visual aura	Present	6	40.233	0.8710	t=4.61 p=0.001
	Absent	6	42.450	0.7944	

Table 20 illustrates the critical flicker frequency(Hertz) among computer users in subjects with and without aura.

The mean critical flicker frequency among migraineurs with aura is 40.233+/-0.8710. The mean critical flicker frequency among migraineurs without aura is 42.450+/-0.7944. The observed difference is statistically significant($p<0.05$). Thus among computer users the critical flicker frequency is lower in migraineurs with aura.

DISCUSSION

The human visual system processes information from the environment in three ways namely, spatially, temporally and chromatically.[6] The spatial responsiveness reflect the functioning of parvocellular neurons.[7] The temporal responsiveness reflect the functioning of magnocellular neurons.[7] The human visual system appears to be involved both in migraine mechanism as well as in its clinical effect.[8]

Precortical dysfunction of spatial and temporal visual processing in migraine has been demonstrated by Coleston et al.[7] They used background modulation method to describe changes in both spatial and temporal filter mechanisms (ST-1 response is spatial and ST-2 response is temporal). [7] In migraineurs, similar studies have been done earlier, but many of them have investigated responses to spatial stimuli, rather than temporal stimuli.[6] Khalil et al investigated temporal contrast sensitivity in migraine and found that it was reduced in migraineurs with aura but not

in migraineurs without aura.[6] Critical flicker frequency is a much simpler test used to assess the temporal responsiveness of the visual system.[22,45]

The current study aimed at evaluating the temporal responsiveness of the visual system through critical flicker frequency. The group critical flicker frequency was highest for control subjects (45.663+/-1.898), the next highest critical flicker frequency was obtained from migraineurs without aura (42.227+/-0.5017) and the lowest critical flicker frequency was obtained from migraineurs with aura (40.363+/-0.8838) ; the observed difference between each of the three subgroups was statistically significant. There were no confounding variables to alter the mean critical flicker frequency in the three groups in the form of age of subject, age of onset of migraine, family history of migraine. Previous studies suggest a decrease in critical flicker frequency with age, and this may be due to differences in target luminance and the presence of early and or subtle ocular disease.[26]

Kowacs et al[23] who in an earlier study analysed critical flicker frequency in migraineurs found that the healthy controls had the highest critical flicker frequency while the migraineurs with aura had the lowest critical flicker frequency and migraineurs without aura had an

intermediate critical flicker frequency and the difference in the three groups were statistically significant.

Coleston et al analyzed the temporal responsiveness of the visual system through background modulation method[7] and critical flicker frequency method.[6] He found that migraineurs had a lower critical flicker frequency than controls. However in the later test he found that the observed difference reached statistical significance only in the migraineurs without aura versus control group. Data from his study highlighted the possibility that visual processing in migraineurs without aura is as problematic and warrants as much investigation as visual processing in migraineurs with aura.

So, analysis of the data from our study as well as comparing it with previous studies reveal that the temporal responsiveness of the visual system is impaired in migraineurs.

The possible pathophysiological mechanisms for the same could be due to (i) some intrinsic abnormality of the magnocellular pathways in migraine (ii) the functional integrity of the pathways may in some way be directly compromised by repeated migraine attacks and (iii) given the existence of rich back projections from the striate cortex to the lateral

geniculate nuclei, the cortical disruptions during the migraine attack may cause retrograde geniculate disturbances as has been interpreted from earlier studies.[7]

Correlation of critical flicker frequency with MIDAS score revealed lower critical flicker frequency in subjects with greater migraine disability in both subgroups (with aura and without aura). In subjects with similar MIDAS score the critical flicker frequency was lower in migraineurs with aura than migraineurs without aura.

Studies in the past have analysed migraine induced by visual stimuli.[20,51] A recent survey conducted in France have analysed four different light stimuli among migraine headache precipitants namely, computer screen, sunshine, dazzling light and neon light.[20] Flickering light stimulation can induce nausea and irritability and may be followed by migraine headaches.[25] However none of the above studies have analyzed temporal responsiveness of the visual system in patients with migraine induced by visual stimuli. A single anecdotal report alone has analysed the critical flicker frequency in such a patient and a change of frequency of computer screen after the analysis of critical flicker frequency in that patient lead to the resolution of the headache.[24] The

current study shows that subjects who had a visual trigger at the onset of migraine headache had a lower critical flicker frequency in both subgroups (with aura and without aura). Secondly among all subjects who had a visual trigger at the onset of migraine, migraineurs with aura had a lower critical flicker frequency than those who did not have aura. This shows that it could be postulated that impaired temporal responsiveness of the visual system could indeed be one of the factors responsible for visual stimuli triggering the migraine headache. However computer usage or non-usage did not show any difference in critical flicker frequency in both subgroups although among computer users, the critical flicker frequency was lower in migraineurs with aura than in those without aura.

Future studies in the above directions could lead to more avenues in the management of migraine headache - one through identifying specific light frequencies that trigger migraine and preventing migraine headache by filtering the specific light frequencies through stained glasses which has been tried earlier[24] and secondly modifying the frequencies of light sources such as computer screens.

SUMMARY AND CONCLUSION

The temporal responsiveness of the visual system is reduced in migraineurs. This is comparable with most studies conducted earlier.

The critical flicker frequency is lowest in migraineurs with aura followed by migraineurs without aura and highest in controls. The observed difference in the three groups is statistically significant.

The temporal responsiveness of the visual system is lowered in migraineurs whose migraine headache is triggered by visual stimuli. Among the sub groups whose migraine headache is triggered by visual stimuli, temporal responsiveness is lower in migraineurs with aura compared to migraineurs without aura.

BIBLIOGRAPHY

1. Abu-Arefeh I, Russell G. Prevalence of headache and migraine in school children. BMJ 1994; 309 (6957) : 765-9.
2. Bigal ME, Lipton RB and Winner P. Migraine in adolescents: association with socioeconomic status and family history. Neurology 2007 ; 69 : 16-25.
3. Brennan KC, Romero – Reyes M and Lopez Valtes HE. Reduced threshold for cortical spreading depression in female mice. Annals of Neurology 2007 ; 6 : 603-6.
4. Burton WN, Conti DJ, Chen CY, et al. The economic burden of lost productivity due to migraine headache: a specific worksite analysis. J Occup Environ Med 2002 ; 44 : 523-529.
5. Chronicle EP, Mulleners WN. Visual system dysfunction in migraine: a review of clinical and psychophysical findings. Cephalalgia 1996 ; 16 : 525-35.
6. Coleston DM, Kennard C. Responses to temporal visual stimuli in migraine: the critical flicker fusion test. Cephalalgia 1995 ; 15 : 396-8.

7. Coleston DM, Chronicle E, Kennard C. Precortical dysfunction of spatial and temporal visual processing in migraine. Journal of Neurology, Neurosurgery & Psychiatry 1994 ; 57 : 1208-11.
8. Coleston DM, Kennard C. Visual changes in migraine : indications of cortical dysfunction. Cephalalgia 1993 ; Suppl 13 :11
9. Cutrer FM, Sorensen AG and Weisskoff RM. Perfusion-weighted imaging defects during spontaneous migrainous aura. Annals of Neurology 1998 ; 43 : 25-31.
10. Dahlof CG and Solomon GD. The burden of migraine to the individual sufferer : a review. European Journal of Neurology 1998 ; 5 : 525-533.
11. Debney LM. Visual stimuli as migraine trigger factors. In : Rose FC, editor. Progress in Migraine Research II. London : Pitman, 1984 : 30-54.
12. Diamond S, Bigal ME, Silberstein S, et al. Patterns of diagnosis and acute and preventive treatment for migraine in the United States : results from the American migraine prevalence and prevention study. Headache 2007 ; 47 : 355-363.

13. Edmeads J, Mackell JA. The economic impact of migraine : an analysis of direct and indirect costs. Headache 2002 ; 42 : 501-509.

14. Elston Lafata J, Moon C, Leotta C, et al. The medical care utilization and costs associated with migraine headache. J Gen Intern Med 2004 ; 19 : 1005-1012.

15. Evans RW, Lipton RB, Ritz KA, et al. A survey of neurologists on self-treatment and treatment of their families. Headache 2007 ; 47 : 58- 64.

16. Goadsby PJ, Ferrari MD, Cesyani A, et al. Randomised double – blind, placebo controlled proof-of-concept study of the cortical spreading depression inhibiting agent tonaberasat in migraine prophylaxis. Cephalalgia 2009 : 29

17. Hadij khani N, Sanchez del Rio M, Wu, et al. Mechanisms of migraine aura revealed by functional MRI in human visual cortex. Proc Natl Acad Sci. USA. 2001 ;.98 : 4687-4692.

18. Hay KM, Mortimer MJ, Barker DC, Debney LM and Good PA. 1044 women with migraine: the effect of environmental stimuli. Headache 1994 ; 34 : 166-8.

19. Headache classification committee of the International Headache society. The International classification of Headache disorders. Cephalalgia 2004 ; 24 (suppl 1) : 1-160.

20. Henry P, Auray JP, Gandin AF, Datrigues JF, Duru G and Lanteri Minet M. Prevalence and clinical characteristics of migraine in France. Neurology 2002 ; 59 : 232-37.

21. Hu XH, Markson LE, Lipton RB, et al. Burden of migraine in the United States: disability and economic costs. Archives of Internal Medicine 1999 ; 159 : 813-818.

22. Kaplan E and Shapely RM. X and Y cells in the lateral geniculate nucleus of macaque monkeys. J Physiology 1982 ; 330 : 125-43.

23. Kowacs PA, Piovesan EJ, Werneck LC, Fameli H, Zani AC and da SilvaHP. Critical flicker frequency in migraine. A controlled study in patients without prophylactic therapy. Cephalalgia 2004 ; 25 : 339-343.

24. Kowacs PA, Piovesan EJ, Werneck LC, Fameli H, Pereira da Silvas HP. Headache related to a specific screen flickering frequency band. Cephalalgia 2004 ; 24 : 408-410.

25. Kowacs PA, Piovesan EJ, Fameli H, Silva HP, Zani AC and Werneck LC. Critical flicker frequency- a study comparing migraineurs with and without aura to normal controls. Neurology 2003 ; 60 (suppl 1) : A406.

26. Lachenmayr BJ, Kojetinsky S, OstermaierN, Angstwurn K, Vivell P, Schaumberger M. The different effects of ageing on normal sensitivity in flicker and light sense perimetry. Invest Ophthal Vis. Sci. 1994 ; 35 : 2741-48.

27. Lasheley KS. Patterns of cerebral integration indicated by the scotomas of migraine. Arch Neurol Psychiatry 1941 ; 46 : 331-9

28. Lauritzen M. Pathophysiology of the migraine aura : the spreading depression theory. Brain 1994 ; 117 : 199-210.

29. Leao AAP. Spreading depression of activity in cerebral cortex. J Neurophysiology 1944 ; 7 : 359 – 90.

30. Legg N and Khalil N. Visual dysfunction in migraine with aura. Cephalalgia 1995 ; 15 : 536.

31. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence disease burden, and the need for preventive therapy. Neurology 2007 ; 8 : 343-49.

32. Lipton RB, Bigal ME, Kolodner K, et al. The family impact of migraine population based studies in the USA and UK. Cephalalgia 2003 ; 23 : 429-40.

33. Lipton RB, Diamond S, Reed M, et al. Migraine diagnosis and treatment : results from American Migraine Study II. Headache 2001 ; 41 : 638-645.

34. Lipton RB, Stewart WF, Simon D, et al. Medical consultation for migraine : results from the American Migraine Study II. Headache 1998 ; 38 : 87-96.

35. Lipton RB, Stewart WF, Von Korff M, et al. Burden of migraine : societal costs and therapeutic opportunities. Neurology 1997 ; 48 Suppl 3 : S4-S9.

36. Lyngberg AC, Rasmussen BK, Jorgenesen et al. Incidence of primary headache : a Danish epidemiologic follow up study. American Journal of Epidemiology 2005 ; 161(11) : 1066-73.

37. MacGregor EA, Brandes J, Eikermann A, et al. Impact of migraine on patients and their families: the Migraine And Zolmitriptan Evaluation (MAZE) survey–Phase III. Curr Med Res Opin 2004 ; 20 : 1143-50.

38. Marcus DA and Soso MJ. Migraine and stripe induced visual discomfort. Brain 1984 ; 107 : 989-1017.

39. Olesen J, Freiberg L, Skhoj – Olesen T, et al. Timing and topography of cerebral blood flow, aura and headache during migraine attacks. Annals of Neurology 1998 ; 28 : 791-8.

40. Olesen J, Larsen B and Lauritzen M. Focal hyperemia followed by spreading oligemia and impaired activation of regional cerebral blood flow in classic migraine. Annals of Neurology 1981 ; 9 : 344-52.

41. Osterhaus JT, Gutterman DL, Plachetka JR, et al. Healthcare resource and lost labour costs of migraine headache in the US. Pharmacoeconomics 1992 ; 2 : 67-76.

42. Rasmusen BK, Olesen J. Migraine with aura and migraine without aura : an epidemiological study. Cephalalgia 1992 ; 12 : 221-8

43. Read SJ, Smith MI, Hunter AJ et al. SB – 220453, a potential novel antimigraine compound, inhibits nitric oxide release following induction of cortical spreading depression on the anaesthetized cat. Cephalalgia 1999 ; 20 : 92-99.

44. Robbins L. Precipitating factors in migraine : a retrospective review of 494 patients. Headache 1994 ; 34 : 214-6.

45. Schiller PH and Malpeli JG. Functional specificity of lateral geniculate nucleus laminae of the rhesus monkey. J Neurophysiology 1978 ; 41 : 788-97.

46. Stewart WF, Wood GC, Razzaghi H, et al. Work impact of migraine headaches. J Occup Environ Med 2008 ; 50 : 736-745.

47. Stewart WF, Bigal ME, Lipton RB, et al. Lifetime migraine incidence. Results from the American Migraine Prevalence and Prevention study. Headache 2005 ; 46 : 52.

48. Smith MI, Read SJ, Chan WN et al. Repetitive cortical spreading depression in a gyrencephalic feline brain : inhibition by the novel benzoylamino -benzopyran SB-220453. Cephalalgia 2000 ; 20 : 546-53.

49. Stovner L, Hagen K, Jensen R, et al. The global burden of headache prevalence and disability world wide. Cephalalgia 2007; 27(3) : 193-210.

50. Stang PE, Crown WH, Bizier R, et al. The family impact and costs of migraine. Am J Manag Care 2004 ; 10 : 313-320.

51. Van den Bergh V, Amery WK and Waelkens J. Trigger factors in migraine : a study conducted by the Belgian Migraine society. Headache 1987 ; 27 : 191-6.

52. Van Harreveld A, and Stamm JS. Cortical responses to metrazol and sensory stimulation in the rabbit. EEG Clin Neurophysiol 1995 ; 7 : 363-70.

53. Walter G Bradley et al Neurology in Clinical practice. V edition. Volume II : 2026-2033.

54. Watanabe H, Kuwabara T, Ohkubo M, et al. Elevation of cerebral lactate detected by localized 1H-magnetic resonance spectroscopy in migraine during the interictal period. Neurology 1996 ; 47 : 1093-1095.

55. Welch KMA and Ramadan NM. Mitochondria, magnesium and migraine. J Neurol Sci 1995 ; 134 : 9-14.

56. Wilkins A. Visual Stress. Oxford : Oxford University Press, 1995.

57. Wilkins A, Nimmo Smith I, Tait A, Mc mannus C, Della Sala S, Tilley A et al. A neurological basis for visual discomfort. Brain 1984 ; 107 : 989-1017.

58. Worthern DM. The eye as a source of headache. In: Dalesio DS, editor. Wolff's headache and other head pain. 4th ed. New York : Oxford University Press, 1980: 388-402.

ANNEXURE I

PROFORMA

SERIAL NUMBER_____ DATE_____

NAME _____

AGE _____ Male / Female Ht_____Wt_____

PHONE _____CELL_____

ADDRESS_____
_____
_____
_____
_____
_____
_____

Occupation_____

Hours of work_____
(per week)

Hours of computer use_____
(Per week)

Hours of television usage_____
(per week)

Headache History
Age of onset of headache _____

Number of years of headache _____

Average number of headaches
per month _____

Location □ Temporal Rt/Left □ Occipital □Top of head □Back of neck

Description □Throbbing □Pressure like □Sharp □Burning □dull □aching

□tightness in the back of neck □other

Aura □visual □other

Associated □Nausea □photophobia □vomiting □numbness

Symptoms □dizziness □ vision changes □other

Duration of Headache(per episode) :

Visual Triggers :

MIDAS SCORE :

Past Medical History: □Asthma □ Coronary artery disease □HTN

□Diabetes □Epilepsy □Other

Past Surgical History:

Head injury: □yes □no

Family history of migraine: □mother □father □brother □sister □other

Diet History: □Alcohol □coffee □tea □nicotine

Menstrual History: □Cycles regular □irregular □birth control pills

Ophthalmological History: □ refractory error □other ocular disorders

Drug History :

General examination :

Blood .Presssure :

Pulse Rate:

CNS Examination :

CFF Measurements:
(Average)

ANNEXURE II

MIDAS QUESTIONNAIRE

INSTRUCTIONS:

Please answer the following questions about ALL the headaches you have had over the last 3 months.

1. On how many days in the last 3 months did you miss work or school because of your headaches?

2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? (Do not include days you counted in question 1).

3. On how many days in the last 3 months did you not do household work because of your headaches?

4. How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches? (Do not include days you counted in question 3).

5. On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches?

A. On how many days in the last 3 months did you have any headache?
(if a headache lasted more than one day, count each day)

B. On a Scale of 0-10 on average, how painful were these headaches?

Grading system for the MIDAS Questionnaire

MIDAS	Definition	Score
I	Minimal or infrequent disability	0–5
II	Mild disability	6–10
III	Moderate disability	11–20
IV	Severe disability	21+

S.No.	Name	Age	Sex	Occupation	Work hours/ week	Computer use	Age of onset	Duration of Migraine (years)	Avg. no. of episodes per month	Aura	Duration of each Episode	MIDAS	Family history	Critical Flicker Freqency (hertz)	Visual trigger	Region of Headache
1	Sarala	21	female	cable tv officer	48		20	1	3	visual	6 hours	2	nil	40.1	Present	r temporal
2	Sandhya	23	female	housewife			19	4	3	visual	12hours	2	mother brother	40.7		l temporal
3	Indhra	35	female	housewife		5hrs/wk	33	2	4	visual	10 hours	2	nil	40.5		R temporooccipital
4	Sankaraeswari	38	female	packing work	54		36	2	5	visual	5 hours	3	nil	39.2	Present	l temporal
5	Kedeeeswari	22	female	tailor	3	7hrs/wk	20	2	5	visual	15 hours	2	nil	40.2		temporo occipital
6	Ezhil arasu	35	male	auto driver	60		31	4	4	visual	12 hours	2	nil	40	Present	l temporal
7	Nasreen	18	female	student	36		15	3	3	visual	5 hours	2	nil	39.8	Present	l temporal
8	Mallika begum	40	female	beedi worker	36		37	3	2	visual	6 hours	1	nil	41.8		r temporal
9	Raman	26	male	welding work	30		25	1	4	visual	6 hours	2	nil	40.3		l temporal
10	Manimegalai	39	female	house maid	48		34	5	4	visual	6hours	2	nil	40.3		l frontooccipital
11	Satish	18	male	student	35	4hrs/wk	17	1	2	visual	6 hours	1	mother	41.7		l temporal
12	Lalitha	17	female	housewife			16	1	7	visual	5 hours	3	nil	39.1	Present	r temporofrontal
13	Selvi	41	female	farmer	28		39	1	3	visual	6 hours	2	nil	40.5		l parietal
14	Rajeswari	35	female	housewife			33	2	4	visual	18 hours	2	nil	40.8		r temporal
15	Lakshmi	40	female	coolie	8		38	2	2	visual	24 hours	1	nil	41.9		r temporal
16	Sarala	27	female	cottage ind.	48		24	3	6	visual	12hours	3	nil	39	Present	r frontotemporal
17	Thangarathinam	37	female	housewife			34	2	3	visual	5hours	1	nil	41.9		l temporal
18	Malar	29	female	housewife			26	3	2	visual	6 hours	1	nil	41.6		r temporoparietal
19	Karthikaveni	25	female	housewife			24	1	6	visual	7 hours	3	nil	39.1	Present	l temporal
20	Rekha	26	female	housework			24	2	4	visual	6 hours	2	nil	40.9		l temporal
21	Vinoth kumar	20	male	packing work	10		18	2	2	visual	10 hours	1	nil	41		r temporal
22	Sarasu	40	female	house maid	54		40	1/2	4	visual	6 hours	2	nil	40.3		l parietal
23	Akash	13	male	student	40	2hr/wk	13	1/12	3	visual	6 hours	2	nil	40.2	Present	r temporal
24	Janani	14	female	student	40		11	3	2	visual	4 hours	1	nil	41.2		l occipitoparietal
25	Manonmani	39	female	broker			34	5	8	visual	12 hours	3	mother	39.3		l parietal
26	Kalaivani	29	female	house maid	24		25	4	4	visual	7 hours	2	mother	40.5		l temporal
27	K. Sahayam	15	male	student	40	7hrs/wk	11	4	6	visual	10 hours	3	nil	39.7		l temporal
28	Paranthaman	32	male	tailor	54		32	1	3	visual	5 hours	2	nil	40.6		l parietal
29	Jeyasubramani	40	male	farmer	24		38	2	6	visual	6 hours	3	nil	39.6	Present	r parietal
30	Renuka	24	female	system operator	60	30hrs/wk	22	2	8	visual	7 hours	3	nil	39.1		l temporal

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1	Vedakani	19	female	student	40	3hrs/wk	16	3	2		4 hours	1	nil	42.9		l occipitotemporal
2	Sridevi	32	female	beautician	40		28	4	3		6 hours	1	nil	42.7		l temporal
3	Parameswari	28	female	housewife			27	1	2		6 hours	1	nil	42.1		r temporal
4	Vinoth	18	male	student	40		15	3	2		5 hours	2	nil	42.2	Present	r parieto temporal
5	Sivakami	40	female	Housewife			39	1	3		10 hours	3	nil	41.5	Present	l temporal
6	Thahira begum	30	female	housewife			28	2	4		18 hours	1	nil	42.6		r temporal
7	Selvi	42	female	pharmacist	40		37	5	2		10 hours	1	nil	42.3		l frontotemporal
8	Ammu	31	female	constr. worker	40		26	5	5		10 hours	2	nil	42.1		l temporal
9	Devi	45	female	housewife			38	7	3		6 hours	3	nil	41.1	Present	l parietal
10	Uma	29	female	nutrition centre	30		27	3	6		10 hours	1	nil	42.7		r parietal
11	Santhoshkumar	13	male	student	60	6hrs/wk	10	3	3		8 hours	1	nil	42.5		l temporal
12	Meena	16	female	student	56		15	1	2		7 hours	1	nil	42.1		r temporal
13	Naveen Raj	13	male	student	70	21h/wk	13	1	4		4 hours	1	nil	42.5		r temporooccipital
14	S Leone	37	male	photographer	12	35h/wk	35	2	4		5 hours	1	nil	43.1		r temporal
15	Dhanabagiyam	42	female	beediworker	36		37	5	3		7 hours	2	nil	42.1		l parietooccipital
16	Menaka	33	male	tailor	21		27	5	5		10 hours	2	nil	41.8	Present	l temporal
17	Abiba	13	female	student	54		12	1	3		6 hours	1	nil	42.3		l temporal
18	Mythili	13	female	student	48		11	2	8		4 hours	1	nil	42		r temporal
19	Amsa	40	female	housewife			35	5	4		6 hours	2	nil	42.1		l temporal
20	Babu	37	male	vessel polisher	60		32	5	2		12 hours	2	nil	42	Present	r temporal
21	Raji	25	female	loader	42		30	5	2		5 hours	2	nil	42.2		r temporal
22	Lakshmi	32	female	housewife			19	3	4		6 hours	1	nil	42.7		l temporal
23	Parvathy	32	female	housewife			27	5	4		7 hours	2	nil	42.2		l temporal
24	Sureshkumar	28	male	office boy	54		22	6	4		6 hours	2	nil	42.1		l temporooccipital
25	Diwakar	14	male	student	54		14	5	3		6 hours	2	father	41.9	Present	l temporal
26	Annalakshmi	21	female	student	21	4h/wk	19	2	2		5 hours	1	nil	42.8		l temporal
27	Manjula	27	female	housewife		7h/wk	23	4	5		6 hours	3	sister	40.9	Present	l occipitotemporal
28	Rose	26	female	housewife			20	6	2		10 hours	3	nil	41.8		l temporal
29	Vijay	16	male	student	54		15	1	2		5 hours	1	brother	42.8		l temporal
30	Menaka	27	male	housewife			23	4	3		6 hours	1	nil	42.7		l frontal

S.No.	Name	Age	Sex	Occupation	Work hours/ week	Computer use	Age of onset	Duration of Migraine (years)	Avg. no. of episodes per month	Aura	Duration of each Episode	MIDAS	Family history	Critical Flicker Freqency (hertz)	Visual trigger	Region of Headache
1	Suresh	21	male	industry worker	40									45.1		
2	Ravi	40	male	mason	60									44.4		
3	Maniarasi	40	female	housewife										45.7		
4	Karthikeyan	39	male	constr. worker	60									44.9		
5	Rajarajeswari	44	female	nurse	36									48.1		
6	Pownu	43	female	housewife										44.9		
7	Dhanasekar	25	male	milk vendor	60									46.3		
8	Kalaivani	21	female	student	30									46.7		
9	Santhanlakshmi	40	female	teacher	48	14h/wk								44.9		
10	Mumtazbegum	41	female	beediworker	48									45.3		
11	Prema	32	female	housewife										45.7		
12	Muniamma	35	female	Limestone worker	60									45.4		
13	Baby	24	female	nurse	36									45.8		
14	Revathy	24	female	nurse	36									44.7		
15	Parivallal	22	male	nurse	36									45.6		
16	Shalu	19	male	uniform supplier	48									45.3		
17	Thangeswaran	20	male	auto driver	60									47.9		
18	Sathyan	21	male	student	40	10h/wk								43		
19	Kalaivani	25	female	housewife										44.1		
20	Santhi	17	female	tailor	24									47.2		
21	Kasthuri	24	female	house maid	18									46.3		
22	Murugan	30	male	steel industry	60									45.9		
23	Kandasamy	32	male	electrician	60									46.1		
24	Selvi	23	female	housemaid	24									44.4		
25	Indirani	18	female	student	40									45.9		
26	Jai ganesh	20	male	student	40	10h/wk								45.6		
27	Duraipandi	28	male	loader	60									46.2		
28	Chellamma	21	female	housemaid	21									43.9		
29	Saleem	30	male	auto driver	48									47.9		
30	Sundar	24	male	artist	35									46.7		